

**Appl. No.** : **09/595,096**  
**Filed** : **June 15, 2000**

## **REMARKS**

The applicant initially wishes to thank the Examiner for the time taken during the interview of February 23. The Examiner's comments were very helpful.

The Applicants have amended Claims 1 and 21 to specify that the claimed method and system are directed to docking a ligand to a protein for selecting one or more conformations of a ligand likely to bind to a protein. Steps for calculating a score for an optimized protein-ligand complex using one or more potential functions and selecting one or more optimized ligand positions based on the score are included. Support for selecting one or more conformations of a ligand may be found in the specification, for example, at page 28, paragraph 1. Support for calculating a score using one or more potential functions may be found in the specification, for example, from page 17 to page 20. Support for selecting one or more optimized ligand positions based on the score may be found in the specification, for example, at page 28, paragraph 1 ("scoring function used...as an initial filter to select only a few docked conformations."). Claims 11-20 have been cancelled without prejudice to pursuing these claims in a divisional, continuation, or continuation-in-part application.

Claims 1-10 and 21-30 remain pending in the application. The Applicants have carefully considered all of the Examiner's rejections but respectfully submit that the claims are allowable for at least the following reasons.

### Rejections under § 112 – Written Description

The Examiner rejected Claims 1-30 under 35 U.S.C. § 112, ¶ 1 as failing to comply with the written description requirement. The Examiner asserted that a method of identifying a ligand that binds to a protein constituted new matter. The Applicants have herein amended the claims so that they are now directed to docking a ligand to a protein for selecting one or more conformations of a ligand likely to bind to a protein, thereby obviating the Examiner's rejection. Written description support for the claim amendments are set forth above.

### Rejections under § 101 – Method Claims 1-10

In the Office Action, the Examiner suggested that "a method of ranking conformations and selecting a conformation or conformations of a ligand that are likely to bind to a binding site

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or hot spot of a protein MAY be considered statutory and MAY be useful.” Office Action, page 4. The Applicants thank the Examiner for attempting to advance prosecution and providing this suggestion. The Applicants have accordingly amended Claims 1-10 so that they are directed to docking a ligand to a protein for selecting one or more conformations of a ligand likely to bind to a protein. As indicated in the specification, this method provides for the selection of “well docked positions” for a ligand. Specification, page 28, paragraph 1. The applicants note also that methods of docking ligands to proteins have well known utility. For example, in the specification on page 2, it is stated that “molecular docking can be a useful tool for prioritizing screening efforts.” Support for this statement is provided by references cited in the specification and by the Introduction section of the new reference (discussed further below) sent by the Examiner with the Advisory Action.

Accordingly, the invention claimed in Claims 1-10 provides concrete, tangible, and useful results and is therefore directed to statutory subject matter, as referred to by the Examiner.

Rejections under § 101 – Mean-Plus-Function Claims 11-20

In the Office Action, the Examiner argued that the means-plus-function limitations in Claims 11-20 were either duplicative with Claims 21-30 or directed to a non-statutory program of instructions. The Applicants have cancelled Claims 11-20, thereby obviating the rejection of those claims.

Rejections under § 101 – Storage Device Claims 21-30

The Examiner has previously found that Claims 21-30 are directed to statutory subject matter and did not reject the claims on those grounds. *See June 2, 2004 Office Action.* As noted above and suggested by the Examiner, Claims 21-30 as amended herein are useful for selecting one or more conformations of a ligand likely to bind to a protein. Accordingly, it is respectfully submitted that Claims 21-30 are in condition for allowance.

Comments Regarding New Reference

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The Examiner has cited in the Advisory Action the reference QXP: Powerful, rapid computer programs for structure-based drug design. In this reference, atoms of ligand conformations are not matched to hot spots in the protein binding pocket to find an initial ligand-protein complex. Claims 1 and 21 have been amended to clarify this distinction. Claims 1 and 21 now recite that the hot spots are matched “to initially position said at least one conformation of said ligand as a rigid body into said binding site so as to obtain at least one position of the ligand relative to the protein in a protein-ligand complex.” Support for this limitation may be found on page 15, second full paragraph. In contrast, the QXP method does not position a previously defined ligand conformation as a rigid body onto hot spots of the binding pocket, but states at the bottom of page 339, second column, that “the ligands were randomly rotated and translated and the torsion angles were randomized before docking.”

It is respectfully submitted that the claims are patentable over this reference.

### **CONCLUSION**

The Applicants respectfully submit that they have overcome all of the Examiner's rejections by the amendments and remarks herein. Accordingly, the Applicants respectfully submit that the pending claims are allowable and request timely issuance of a Notice of Allowance.

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Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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